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# Intertest Variability of Echocardiographic and Chest X-Ray Measurements: Implications for Decision Making in Patients With Aortic Regurgitation

JADWIGA SZLACHCIC, MD,* BARRY M. MASSIE, MD, FACC,*
BARRY GREENBERG, MD, FACC,† DAVID THOMAS, PHD,† MELVIN CHEITLIN, MD, FACC,*
J. DAVID BRISTOW, MD, FACC,† with the assistance of CHRISTINE ANDERSON, BA,
REX SOLIN, BA, ROB McDONALD, BA, NINA TOPIC, RN, DEIRDRE SMIENCZUK, RN

*San Francisco, California and Portland, Oregon*

**Echocardiograms and chest X-ray examinations are commonly employed for serial measurements of left ventricular size and function in patients with chronic aortic insufficiency and often support or even determine therapeutic decisions. This study was undertaken to assess the intertest variability of these measurements made from M-mode echocardiograms and X-ray films performed 3 months apart without intervening clinical or therapeutic changes in 22 patients with significant but asymptomatic aortic insufficiency. End-diastolic and end-systolic dimensions, fractional shortening and cardiothoracic ratios were measured by the same reader, with the initial and 3 month tests being read both independently and together for comparison. The mean values for the initial and 3 month studies were similar, but the intertest variability was substantial, especially when the two tests were read independently. The 95% prediction limits are approximately 50% smaller when the serial studies are read together for comparison. The coefficient of variation for end-diastolic and end-systolic dimensions was 6.1 and 10.1%, respectively, and that for fractional shortening was 17.1%.**

**These findings translate into 95% level prediction limits exceeding ± 8 mm for left ventricular dimensions and 0.12 for fractional shortening; changes on serial evaluations would have to exceed these values to be considered with a high degree of certainty to represent more than random variability. Although this variability may reflect a number of biologic and technical factors, it emphasizes the need to be cautious in making decisions based solely on changes between two tests, particularly if they are not evaluated together.**

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Serial echocardiograms and chest X-ray examinations are often employed to determine and monitor therapy in patients with chronic aortic regurgitation (1–6). Progressive left ventricular dilation or functional deterioration are commonly considered indications for surgical intervention. However, the proper interpretation of changes on repeat studies requires knowledge of the variability of these measurements, due to both spontaneous fluctuations over time (temporal variability) and limitations of reproducibility (measurement variability). Therefore, the objective of this study was to examine the variability of M-mode echocardiographic and chest X-ray measurements of left ventricular size and function on repeat studies over a short time interval in asymptomatic, clinically stable patients with moderate or severe aortic insufficiency. An additional goal of this study was to compare the variability of these measurements when the two studies were read independently and when they were read together, because the practicing physician often deals with data obtained in both of these ways.

From the *Cardiology Service of the Veterans Administration Hospital and the Department of Medicine and Cardiovascular Research Institute of the University of California, San Francisco, California and †Oregon Health Sciences University, Portland, Oregon. This work was supported by Grants HL28146 and GM07546 from the National Heart, Lung, and Blood Institute, Bethesda, Maryland and by the Veterans Administration Research Service, Washington, DC.

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Address for reprints: Barry M. Massie, MD, Department of Cardiology (111C), Veterans Administration Medical Center, 4150 Clement Street, San Francisco, California 94121.

## Methods

**Study patients.** The study group comprised 22 patients with chronic aortic regurgitation. There were 19 men and



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3 women with a mean age of 49 years (range 24 to 77). The etiology of aortic insufficiency was thought to be a congenitally bicuspid valve in 11 patients, rheumatic disease in 4, endocarditis in 2 and unknown in 5. All patients had normal sinus rhythm.

Only patients with significant disease, as indicated by the clinical findings of cardiomegaly, widened pulse pressure (> 60 mm Hg) and peripheral signs of aortic regurgitation, were included. To further ensure the hemodynamic significance of the volume overload, all were required to have an increased left ventricular volume by radionuclide angiography (> 110 ml/m$^2$, which is the upper 95th percentile for our laboratory) (7), together with preserved left ventricular function as indicated by a radionuclide ejection fraction greater than 55%. No patient had evidence of other valvular disease, including aortic stenosis, or other cardiac disease. Twelve patients had undergone cardiac catheterization with confirmatory findings. All patients were asymptomatic, clinically stable and, on subsequent serial studies, free of progressive changes in left ventricular size and function during the 9 months after the second echocardiographic study.

These patients were participants in a multicenter trial of hydralazine compared with placebo in asymptomatic aortic insufficiency and were drawn from the placebo group, with their data being provided blindly by the statistical center for this analysis. None of these patients were taking cardioactive or vasoactive medication.

**Measurements.** Each patient underwent echocardiography on two occasions 3 months apart by standard techniques, using dedicated M-mode echocardiographs in 30% of patients and M-mode tracings derived from two-dimensional machines in the remainder. The equipment employed, technologist performing the study, position of the patient and the echocardiographic window were recorded and kept constant. Heart rate was noted from the simultaneously recorded electrocardiogram and blood pressure was measured by sphygmomanometry.

*Measurements of left ventricular end-diastolic and end-systolic cross-sectional diameter,* interventricular septum and posterior wall thickness and left atrial diameter were made on three to five consecutive cycles, using conventional criteria (8), and averaged. Left ventricular fractional shortening was derived from the standard equation.

*A single observer read both the initial and the 3 month study twice.* First, each tracing was read independently without knowledge of the order in which it had been performed or that the two tracings had been obtained from the same patient. On the second occasion they were read together, with the order unknown, and the measurements were made at identical levels in relation to the mitral valve apparatus and employing the same endocardial echoes. The interstudy variability of the two sets of readings was determined and compared. As a reference, two sets of readings obtained on the initial study were used to define the same-observer reproducibility of these measurements. Furthermore, to define interobserver reproducibility, a second observer performed measurements on the initial echocardiograms.

*The same patients also underwent initial and repeat standard posteroanterior chest X-ray examinations.* Cardiothoracic ratios were measured for the two studies, which were read both separately and together by the same observer.

**Statistical methods.** The paired *t* test was used to assess changes in mean values for each variable between the two studies. The standard deviation of the difference between the initial and repeat studies was used to define the variability of the measurements. Likewise, the standard deviation of the difference between the two readings was used to define interobserver and same-observer reproducibility. The statistical significance of the difference of the variances of the paired observations from the independent readings versus readings made together was examined by an appropriate test (9). The variability between studies and between readings was also expressed as the coefficient of variation, the standard deviation of the difference divided by the mean value. This dimensionless index facilitates comparisons between measurement variability in the present study and in previous studies. The points derived from the pairs of readings were also fit to the line that minimizes the sum of the squared perpendicular distances of (x,y) data points (10). This principal component approach treats the two readings symmetrically, in contrast to the least squares linear regression approach. Furthermore, the resultant fitted line would reduce to the identity line ($y = x$) if and only if the means were equal and the variances were equal. Hence, the statistical significance of the deviation of the fitted line from the line of identity was determined by using the paired *t* test for comparison of means and the test for comparison of variances (9).

## Results

**Interstudy variability.** Table 1 shows the mean heart rate and systolic and diastolic blood pressures recorded at the time of the two echocardiograms. There were no significant changes between the two studies in the mean values of these measurements. The standard deviations of the differences were quite large: 16 beats/min for heart rate and 15 and 13 mm Hg for systolic and diastolic blood pressure, respectively, indicating that some individuals exhibited substantial variability in those indexes. The coefficients of variation were 21% for heart rate and diastolic blood pressure and 11% for systolic pressure.

*The measurements obtained from the initial and repeat echocardiograms and chest X-ray films* by the independent and simultaneous readings are shown in Table 2. Again, there were no significant changes between the two studies with either measurement procedure. However, the standard

**Table 1.** Heart Rate and Blood Pressure Readings at the Time of the Two Echocardiograms

| | Study 1 | Study 2 | SD of Difference | Coefficient of Variation (%) |
|---|---|---|---|---|
| Heart rate (beats/min) | 78 ± 18 | 76 ± 13 | 16.3 | 21.1 |
| Systolic blood pressure (mm Hg) | 140 ± 22 | 139 ± 23 | 15.3 | 11.0 |
| Diastolic blood pressure (mm Hg) | 61 ± 15 | 60 ± 12 | 12.7 | 21.0 |

None of the interstudy differences in means are statistically significant SD of difference = standard deviation of the difference between the measurements from study 1 and study 2.

deviations of the differences for all the echocardiographic measurements were significantly larger when the two studies were read independently than when they were read together (simultaneous readings). When the two studies were evaluated independently, the standard deviation of the difference for end-diastolic and end-systolic dimension was 4.1 and 4.4 mm, respectively, compared with 1.6 and 1.9 mm when the studies were read side by side (both $p < 0.001$). Therefore, a change greater than 8 mm between two independently read studies is necessary to be 95% confident that it represents an increase or decrease in left ventricular size; if the serial echocardiograms are read together, a change greater than 4 mm can be considered more than random variability.

The large variability in dimensions was associated with a similar variability in fractional shortening, where two standard deviations were greater than 0.12. Significant differences in variability between simultaneous and independent readings were also present for all other echocardiographic measurements. They were most striking for left atrial dimension (standard deviation of 2.4 versus 8.1 mm); for this measurement, independent readings often resulted in analysis of different posterior wall echoes in the two studies.

In contrast to the echocardiographic findings, there was little variability between the two cardiothoracic ratio measurements, whether the X-ray films were read independently or together.

*Figures 1 to 4 present the variability findings in a different format.* Measurements from study 2 and study 1 are plotted together, with the line of identity shown. The 95% prediction band for differences ($y - x$) is drawn around the $y - x$ line based on the variability of ($y - x$) about zero. The interrupted lines are the best fit of the points when the two measurements are treated symmetrically, by employing principal component analysis (see Methods) (10). This line was not significantly different from the line of identity with either procedure for reading the echocardiograms, but the wider prediction bands with the independent readings clearly illustrate the greater potential for random interstudy variability with this approach.

**Same-observer and interobserver reproducibility.** To put the variability in measurements between two different studies into perspective, the reproducibility of sets of measurements made in a single study by the same observer or by different observers was determined (Table 3).

In general, there were only minor differences between the two readings of the same (initial) echocardiogram by observer 1. Only this observer's slight tendency to record a larger end-systolic dimension on the second reading (43 ± 6 versus 44 ± 6 mm, $p < 0.05$) achieved significance. The variability in the two readings of this study was slightly greater than that obtained in reading the two serial echocardiograms side by side.

*When two observers read the first study,* the variability in their measurements tended to be greater than that obtained

**Table 2.** Interstudy Variability of Echocardiographic and X-Ray Film Measurements

| | Independent Readings | | | | Simultaneous Readings | | | |
|---|---|---|---|---|---|---|---|---|
| | Study 1 | Study 2 | SD of Difference | Coefficient of Variation (%) | Study 1 | Study 2 | SD of Difference | Coefficient of Variation (%) |
| LA (mm) | 39 ± 6 | 39 ± 7 | 8.1 | 20.8 | 37 ± 5 | 37 ± 6 | 2.4‡ | 6.5 |
| EDD (mm) | 67 ± 6 | 67 ± 8 | 4.1 | 6.1 | 67 ± 6 | 67 ± 7 | 1.6‡ | 2.4 |
| ESD (mm) | 43 ± 6 | 44 ± 8 | 4.4 | 10.1 | 44 ± 6 | 45 ± 7 | 1.9‡ | 4.3 |
| FS | 0.36 ± 0.06 | 0.34 ± 0.07 | 0.06 | 17.1 | 0.34 ± 0.05 | 0.34 ± 0.04 | 0.02‡ | 5.9 |
| PW (mm) | 12 ± 2 | 12 ± 1 | 1.6 | 13.3 | 12 ± 2 | 12 ± 1 | 0.6† | 5.0 |
| IVS (mm) | 13 ± 3 | 13 ± 2 | 1.8 | 13.8 | 13 ± 2 | 12 ± 2 | 1.0* | 8.0 |
| CT ratio | 0.52 ± 0.06 | 0.51 ± 0.06 | 0.02 | 3.8 | 0.52 ± 0.06 | 0.52 ± 0.07 | 0.03 | 5.8 |

*$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ for independent versus simultaneous readings. No significant difference in the means was found between study 1 and study 2 by either measurement procedure. CT = cardiothoracic; EDD = end-diastolic dimension; ESD = end-systolic dimension; FS = fractional shortening; IVS = interventricular septal thickness; LA = left atrial dimension; PW = left ventricular posterior wall thickness.

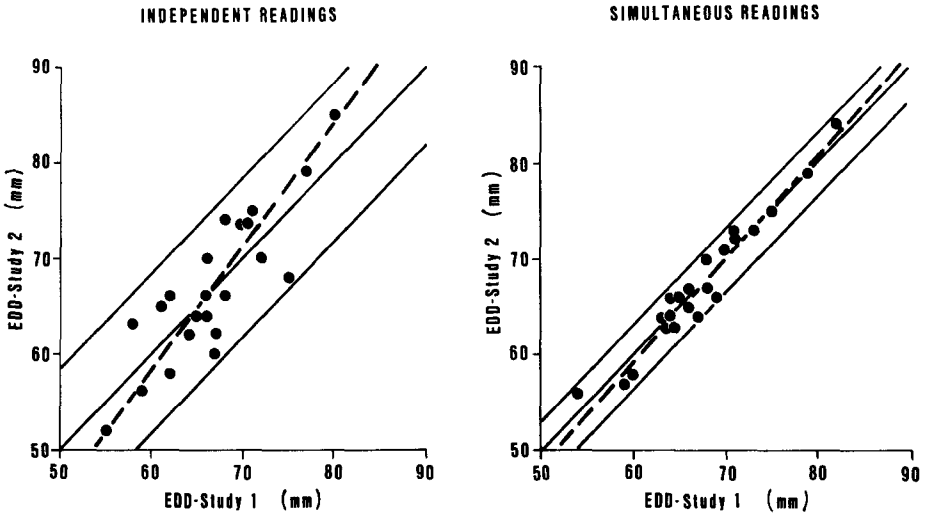


**Figure 1.** Plots of the echocardiographic measurements of end-diastolic dimension (EDD) from the first and second studies. The **left panel** shows the results of the independent readings of the two studies, and the **right panel** shows the results when the studies were read together. The **solid line** is the line of identity. The **interrupted line** is the best fit of measurements determined by principal component analysis (see Methods). The **outer lines** indicate the 95% prediction band for the difference of measurements. Note that although both measurement approaches yield relations between the two sets of readings that do not differ significantly from the line of identity, the variability is much smaller when the studies are read together.

with two readings of the same study by a single observer but less than that seen between serial studies read independently.

## Discussion

It has become standard practice to order serial echocardiograms in patients with clinically important aortic regurgitation (1–6). Although there is still disagreement concerning the optimal timing for valve replacement in asymptomatic or minimally symptomatic patients (3,11–15), most investigators would agree that those with progressive left ventricular dilation or decreasing contractile function warrant special attention and possible early intervention. However, the proper interpretation of serial echocardiographic measurements requires knowledge of their reproducibility (similarity of measurements obtained on the same study) and temporal variability (differences in measurements from two studies separated in time).

**Reproducibility of echocardiographic measurements.** A considerable literature (16–25) exists on the reproducibility and variability of echocardiographic measurements, although many of these studies have focused on normal subjects. Measurement reproducibility reflects a number of factors, such as whether the readings are made by the same or different observers, whether the same views and cardiac cycles are selected for evaluation and whether the measurements are made at the identical phase in the cycle and employ the same echoes. Most investigators (20,22,24) have reported good reproducibility for measure-

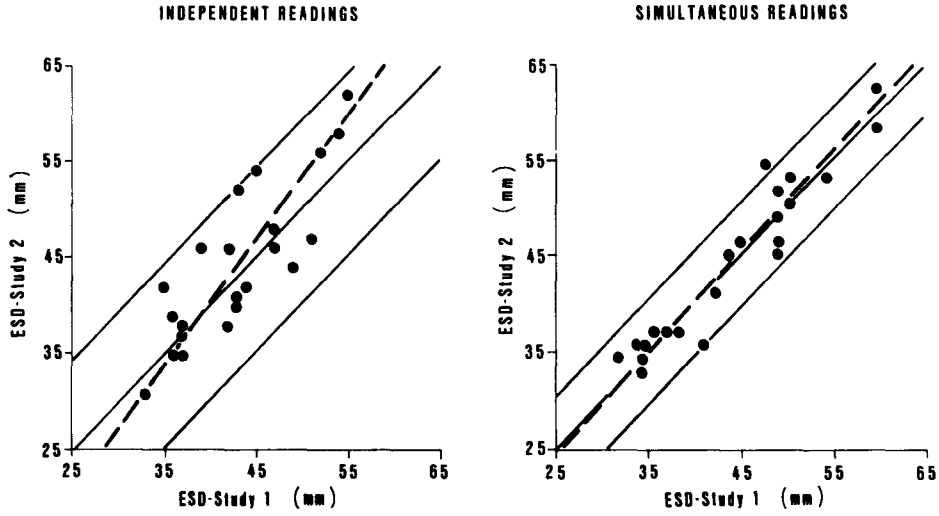


**Figure 2.** Plots of the echocardiographic measurements of end-systolic dimension (ESD). Again, the 95% prediction band is much smaller when the two studies are read together. Format as in Figure 1.

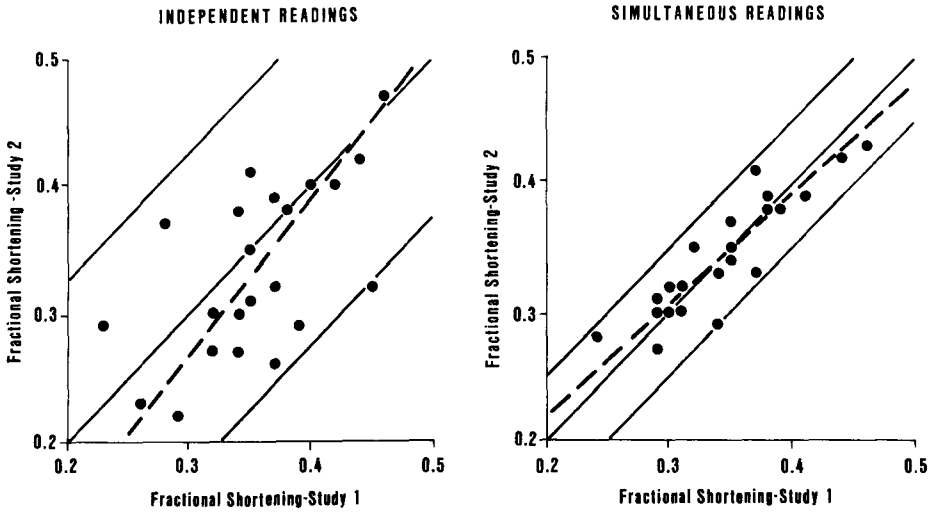


**Figure 3.** Plots of the findings for fractional shortening. The scatter with independent readings is very large. Format as in Figure 1.

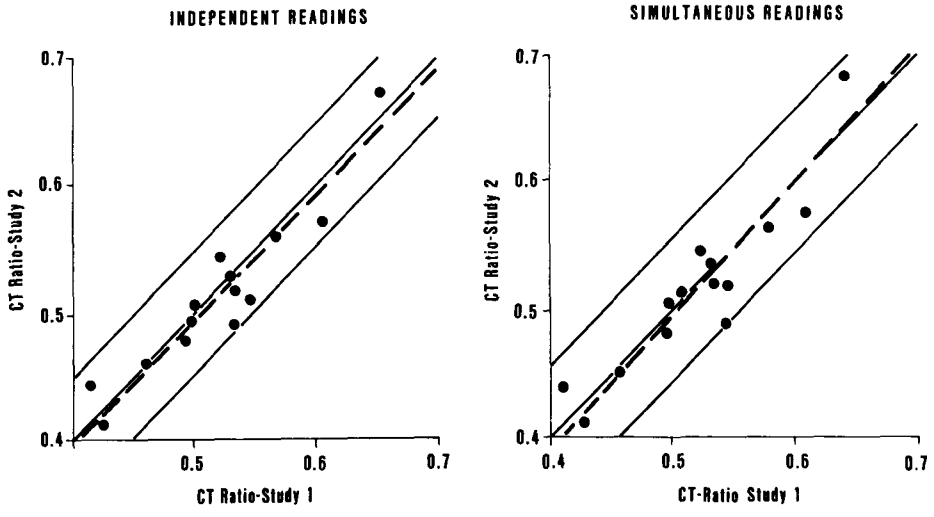


**Figure 4.** Plots of the cardiothoracic (CT) ratio measurements are nearly identical, whether the two studies are read independently or together. Format as in Figure 1.

ments of left ventricular dimensions, with coefficients of variation of 5% or less, especially in normal subjects. As in the present study, same-observer reproducibility is usually superior to interobserver reproducibility (20). Factors such as heart rate (26), phase of respiration (27), patient position and transducer placement (20,24,27,28) have been shown to affect reproducibility. Reproducibility is usually somewhat poorer with calculated fractional shortening, which compounds differences in measured dimensions, and with left ventricular wall thickness and left atrial size, which

**Table 3.** Reproducibility of Echocardiographic and X-Ray Measurements

| | Same-Observer Reproducibility (study 1) | | | | Interobserver Reproducibility (study 1) | | | |
|---|---|---|---|---|---|---|---|---|
| | Reading 1 | Reading 2 | SD of Difference | Coefficient of Variation (%) | Observer 1 | Observer 2 | SD of Difference | Coefficient of Variation (%) |
| LA (mm) | 39 ± 6 | 37 ± 6 | 3.4 | 8 9 | 39 ± 6 | 39 ± 6 | 2.0 | 5.1 |
| EDD (mm) | 67 ± 6 | 67 ± 6 | 2.5 | 3.7 | 67 ± 6 | 67 ± 5 | 3.1 | 4 6 |
| ESD (mm) | 43 ± 6 | 44 ± 6* | 2.5 | 5.7 | 43 ± 6 | 45 ± 5 | 3.3† | 7.5 |
| FS | 0.36 ± 0.06 | 0.34 ± 0.05 | 0.03 | 8.6 | 0.36 ± 0.06 | 0.34 ± 0 06 | 0.06‡ | 17.4 |
| PW (mm) | 12 ± 2 | 12 ± 2 | 0.7 | 5.8 | 12 ± 2 | 12 ± 1 | 1.0 | 8.3 |
| IVS (mm) | 13 ± 3 | 13 ± 2 | 1.3 | 10.0 | 13 ± 3 | 12 ± 2 | 1.5 | 12.0 |
| CT ratio | 0.52 ± 0.06 | 0.52 ± 0.06 | 0.01 | — | — | — | — | — |

*$p < 0.05$ for reading 1 versus reading 2 or observer 1 versus observer 2. †$p < 0.01$, ‡$p < 0.001$, same observer versus interobserver reproducibility. Abbreviations as in Table 2.

**Table 4.** Temporal Variability of Echocardiographic Measurements: Present Findings in Relation to Published Results

| Reference No | Study Patients (no.) | Interval Between Studies | Coefficients of Variation | | | | Comment |
|---|---|---|---|---|---|---|---|
| | | | EDD (%) | ESD (%) | FS (%) | Other (%) | |
| 17 | Normal (5) | 1 Week | 3.4 | 3.3 | 8.4 | | |
| 21 | Normal (15) | 4 Weeks | 3.2 | 4.4 | — | PW = 8, IVS = 10 | 4 Weekly echoes |
| 18 | Mixed (15) | 4 Days | 8 9 | 10 5 | — | | |
| 24 | Normal heart size (12) | Minutes | 1.8 | — | — | | |
| 24 | Enlarged heart (12) | Minutes | 4.6 | — | — | | |
| 25 | Normal (10) | 3 Weeks | 2.3 | 3.2 | 8.1 | | |
| 25 | CCM (10) | 3 Weeks | 3.3 | 3.7 | 9.4 | | |
| 4 | AR (15) | 1 Month | 3 1 | 7.4 | 14.1 | LA = 10.5 | |
| 5 | Mixed valve (12) | 1 Week | 3 | — | 10 | | |
| 23 | CCM (20) | 5 Weeks | 6 | 5 | 19 | | 5 Weekly echoes |
| Present study | AR (22) | 3 Months | 6 1 | 10.1 | 17 1 | LA = 21, IVS = 14, PW = 13 | Echoes read independently |
| Present study | AR (22) | 3 Months | 2.4 | 4.3 | 5.9 | LA = 6.5, PW = 5, IVS = 8 | Echoes read together |

AR = aortic regurgitation; CCM = congestive cardiomyopathy; echo = echocardiogram; other abbreviations as in Table 2.

involve a more difficult selection of endocardial echoes (19,20). Of particular relevance to the present study is the poorer degree of reproducibility in patients with a large heart than in normal subjects, which has been reported by several groups (4,23–25).

**Temporal variability.** In employing the echocardiogram for patient management, the clinician is most interested in changes over time. When serial measurements from studies separated in time are compared, there are additional influences on the degree of variability. Thus, all of the factors that affect measurement reproducibility will be operative, but greater physiologic fluctuations and differences in technique are likely to be present. Table 4 reviews the published data on temporal variability of echocardiographic measurements. Comparing echocardiograms performed days or weeks apart, several workers (17,21,24,25) have reported coefficients of variation of less than 5% for left ventricular dimensions in normal subjects. Again, this variability is often greater in patients with an enlarged heart (4,23–25), which is not surprising because fluctuations in heart rate, blood pressure and volume states are more likely to affect patients with heart disease.

**Findings of the present study.** The present study deals exclusively with patients with aortic regurgitation, the entity for which echocardiography has been most extensively employed in clinical follow-up but one in which physiologic fluctuation might have marked effects. For instance, both heart rate and peripheral resistance are important determinants of regurgitant fraction (29,30). Thus, the task of distinguishing spontaneous variation in measurements from progression of the underlying disease may be difficult.

To ensure the clinical relevance of our results, we evaluated echocardiograms performed 3 months apart. This interval is long enough to permit the types of physiologic changes that might occur during the typical interexamination period of 6 to 24 months but short enough to make clinical progression unlikely in subjects in stable condition. We further limited the likelihood of studying patients with progressive disease by including only asymptomatic individuals who exhibited no subsequent change during careful follow-up. This stability was confirmed by the lack of any significant change in the mean values for left ventricular dimension or function during the 3 month interval. Furthermore, the relation between the two sets of measurements did not differ from the line of identity for any of the variables.

*However, the variability of the measurements between the two studies was considerable.* When the studies were read independently, the coefficient of variation for end-diastolic and end-systolic dimension was 6.1 and 10.1%, respectively, and that for fractional shortening was 17.1%. These findings translate into 95% level prediction limits greater than ± 8 mm for the left ventricular dimensions and 0.12 for fractional shortening; changes on serial evaluations would have to exceed these values to be considered with a high degree of certainty to represent more than random variability.

*The present results are shown in relation to previous reports in Table 4.* Two previous studies (4,5) have examined the temporal variability of echocardiographic measurements in valvular heart disease. Our coefficients of variation for left ventricular dimensions are considerably larger than those reported by Clark et al. (5) for a heterogeneous group of patients with valvular disease and somewhat larger than those noted by McDonald and Jelinek (4) in a more comparable group with aortic insufficiency. Our results are closer to those of Unverferth et al. (23) in patients with dilated cardiomyopathy. Our largest coefficient of variation was found in the left atrial dimension and reflected the use of different posterior wall echoes for analysis. There was also considerable variability in wall thickness measurements.

The present study is, to our knowledge, the first to ex-

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amine the differences between measurements obtained by simultaneous readings of serial studies and those resulting from independent readings of the same studies. The former approach produced much less variability, with significantly smaller coefficients of variation. Indeed, the findings with simultaneous readings are more comparable with data previously reported by others (Table 4). Because most of these previous reports did not indicate the procedure employed in making the serial measurements, it is possible that in some of these studies smaller variability was achieved by simultaneous reading of the echocardiograms.

*The difference between the simultaneous and independent readings provides some insight into the sources of the observed variability.* The simultaneous reading procedure minimizes many of the factors that influence measurement reproducibility, facilitating the use of equivalent levels and projections and aiding in the choice of comparable endocardial echoes. The latter is particularly important in measurements of left atrial dimension and myocardial wall thickness. It is noteworthy that the variability between the simultaneous readings of the studies was less than that seen when the same observer read a single study twice on different occasions or when different observers read the same study. This result suggests that measurement reproducibility, rather than temporal variability, is the major source of variability over time in patients with stable aortic regurgitation. That some further temporal variability should occur in the absence of progressive changes in left ventricular function is also not surprising. Indeed, the variability in heart rate and blood pressure, which are important determinants of ventricular size, exceeded that of the echocardiographic measurements.

**X-ray findings.** In contrast to the echocardiographic findings, there was no difference between the interstudy variability of the X-ray cardiothoracic ratio measurements obtained with independent and simultaneous readings. This probably reflects the single view available and the lesser degree of subjectivity in this measurement. However, this finding should not be interpreted as evidence of superiority of the X-ray examination in following up patients with aortic regurgitation, because it does not permit accurate measurement of left ventricular size and provides no data on left ventricular function.

**Implications.** Our results indicate that in aortic regurgitation, the interstudy variability of echocardiographic measurements is considerable, and this variability may make it difficult to evaluate changes in left ventricular size and function. Management decisions should be made only after full clinical evaluation. If increasing chamber size or decreasing function is considered an indication for surgical intervention, the serial studies should be read together by the same physician, stringent criteria should be employed to define a clinically important change and repeat examinations should be performed.

If the serial studies are not read together, or if decisions are made on the basis of reports from different laboratories, our findings indicate that a 9 mm increase in left ventricular dimensions and a 0.12 decrease in fractional shortening are required. With these wide prediction limits, important deterioration could easily be overlooked in occasional patients. Therefore, we recommend that, whenever possible, measurements on the serial studies be performed simultaneously.

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